

### **REMARKS**

The Office Action of June 30, 2010, has been carefully studied. Claims 11 and 14-21 currently appear in this application. These claims define novel and unobvious subject matter under Sections 102 and 103 of 35 U.S.C., and therefore should be allowed. Applicant respectfully requests favorable reconsideration and formal allowance of the claims.

### **Art Rejections**

Claims 11 and 14-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Watanabe et al., WO 01/02378 in view of Patani et al., *Chem. Rev.*, 1996, 3147-3176.

This rejection is respectfully traversed.

The process claimed herein is for preparing heterocyclic fluoroalkenyl sulfones and sulfoxides by oxidizing heterocyclic fluoroalkenyl sulfides with a salt of peroxomonosulfuric acid. In the declaration of Dr. Shlomo Cohen, filed with the amendment filed April 3, 2009, Dr. Cohen found that in preparing the sulfone from the sulfoxide, in order to complete the reaction, it is critical that the pH of the reaction be above 6, and preferably from 8 to 9. Below pH 6, the reaction does not proceed to termination, resulting in poor yield. When the reaction pH is maintained above 6, the reaction proceeds smoothly to termination under moderate conditions, resulting in high yields and purity of sulfone in a short time. There is nothing in Watanabe that even suggests

conducting the reaction at pH above 6, as the only pH adjustment disclosed in Watanabe is after completion of the oxidation, in the work-up step including isolation, purification, etc. Since it has been demonstrated that the pH of the reaction is critical to the yield and purity of the compound, it is not understood why Watanabe in combination with Patani makes the presently claimed process obvious, since none of them teach this essential feature of the process.

Patani adds nothing to Watanabe because Patani merely relates to the steric properties of substituting hydrogen or fluorine. This has absolutely nothing to do with oxidizing the heterofluoroalkenyl compounds that are the subject of the presently claimed process.

The Examiner alleges that Betterton teaches that at a neutral and alkaline pH that peroxymonosulfate is a faster oxidant than hydrogen peroxide, page 531, second column.

Applicant respectfully disagrees with the Examiner's position. Betterton teaches at page 531, second column, "At neutral pH the second-order constant for oxidation of DMS by  $\text{HSO}_3^-$  is nearly ten times higher than that of  $\text{H}_2\text{O}_2$  and in alkaline solution it could be 3 orders of magnitude higher."

From the above, it follows that Betterton teaches that as the pH rises above neutral, the reactivity rate decreases as compared to  $\text{H}_2\text{O}_2$ . This also supports the instability of  $\text{HSO}_3^-$  at higher pH as discussed in the previous response. Moreover, Betterton merely teaches the greater reactivity of the oxidants, but is silent with respect to yield and purity of the reaction products.

As disclosed in the specification as filed at page 2, lines 11-20:

It has now been found that, surprisingly, the use of salts of peroxomonosulfuric acid of the formula  $H_2SO_5$ , for example, potassium hydrogenperoxomonosulfate,  $KHSO_5$ , as oxidizing agents allows the use of particularly mild conditions. It has been found that, for example, Oxone ® and Caroat® are particularly suitable. It is also to be regarded as surprising that the second step of the oxidization of the sulfoxide to the sulfone, after neutralization of the mixture, proceeds with just as few problems as the first. **It is to be regarded as unexpected in particular that it was not possible to observe any significant oxidation of the double bond of the trifluorobutenyl radical, which is particularly problematic in existing processes.** [emphasis added]

In the declaration submitted with the amendment filed April 3, 2009, Dr. Shlomo Cohen reacted heterocyclic sulfide with a salt of peroxomonosulfuric acid, and then reacted the sulfoxide produced with a salt of peroxomonosulfuric acid to produce a sulfone. Dr. Cohen found that in preparing the sulfone from the sulfoxide, in order to complete the reaction, it is critical that the pH of the reaction be above 6, and preferably from 8 to 9. If the pH is below 6, the reaction does not proceed to termination, resulting in poor yield. By maintaining the pH above 6, the reaction proceeds smoothly to termination under moderate conditions, resulting in high yields and purity of sulfone in a short time.

As noted above, the herein claimed process does not oxidize the double bonds of the heterocyclic trifluoroalkenyl sulfone and sulfoxide. Betterton only discloses the mechanism of transformation of reduced sulfur compounds including alkyl sulfides such as dimethyl sulfide and diethyl sulfide. These alkyl sulfides and sulfoxides are completely different compounds from the heterocyclic trifluoroalkenyl sulfides and sulfoxides treated in the presently claimed process. The alkyl sulfides do not have double bonds that must be protected from oxidization during the process. There is absolutely nothing in Betterton that even suggests that the oxidation of alkyl sulfides would be analogous to the oxidation of heterocyclic trifluoroalkenyl sulfides and sulfoxides.

Moreover, Betterton merely teaches (page 531, second column), "At neutral pH the second-order rate constant for oxidation of DMS by  $\text{H}_2\text{SO}_5^-$  is nearly 10 times higher than that of  $\text{H}_2\text{O}_2$  and in alkaline solution it could be 3 orders of magnitude higher." From this, it follows that Betterton teaches that as the pH rises above neutral pH, the reactivity decreases. This also supports the instability of  $\text{H}_2\text{SO}_5^-$  at a higher pH, as discussed in the previous response.

Additionally, Betterton teaches that the greater reactivity of  $\text{H}_2\text{SO}_5^-$  could make it more attractive than  $\text{H}_2\text{O}_2$  where **rapid reaction** is required [emphasis added].

However, the rapid reaction of  $\text{H}_2\text{SO}_5^-$  as compared to  $\text{H}_2\text{O}_2$  teaches nothing concerning the preventing of yield loss of the reaction. In this respect, the Examiner's attention is directed to paragraph [0005] of the US publication

(page 2, lines 5-11). It should be noted that the rate of the reaction is not necessarily related to the yield of the reaction. Furthermore, the rate of reaction teaches nothing concerning the selectivity of the reaction. It is self-evident that a high yield of pure reaction product is an important characteristic of a process.

One skilled in the art aware of (i) the structural formula of the starting compound of the herein claimed method, (ii) the Betterton reference and (iii) attempting to prevent yield losses which are caused by undesired reactions, would not have been led by Betterton to favor the use of  $\text{H}_2\text{SO}_5^-$ , since Betterton teaches nothing concerning selectivity and yield of the reaction claimed herein.

It should also be noted that the reaction in Betterton, in which DMS serves as a substrate (starting material), has nothing to do with the process claimed herein in which the starting compound contains a double bond that is sensitive to oxidation reactions. One skilled in the art, being aware of the sensitivity of double bonds to oxidation, would not look to Betterton for reaction conditions for compounds having double bonds.

Therefore, it is respectfully submitted that Betterton teaches nothing concerning the unexpected results of high yield and selectivity achieved by the herein claimed process. It is clear that the presently claimed method brings about remarkable improvement in yield and selectivity, which could not be predicted by any of the prior art. All that the prior art suggests is that the

reaction could be made more attractive than  $\text{H}_2\text{O}_2$ , where **rapid reaction** is required [emphasis added].

It should be appreciated that the rapid reaction of  $\text{HSO}_3^-$  as compared with  $\text{H}_2\text{O}_2$  teaches nothing concerning preventing yield loss of the reaction. In this respect, the Examiner's attention is directed to paragraph [0005] of the present specification. It is clear that the rate of reaction is not necessarily directly related to the yield of the reaction. Furthermore, the rate of reaction teaches nothing concerning the selectivity of the reaction.

One skilled in the art aware of (i) the chemical structural formula of the starting compound of the herein claimed process, (ii) the Betterton reference and (iii) attempting to prevent losses caused by undesired reactions, would not have been led by Betterton to favor  $\text{HSO}_3^-$ , since Betterton teaches nothing regarding selectivity and yield of the reaction of the claimed process.

It should be noted that the reaction in Betterton, in which DMS is the substrate (starting material), does not relate to the reaction of the presently claimed process. In which the starting material includes a double bond which is sensitive to oxidation reactions.

### **Double Patenting**

The Examiner has maintained the obviousness-type double patenting rejection of claims 11 and 14-21 as being unpatentable over claim 6 of Watanabe, US 6,734,198 in view of Patani.


This rejection is respectfully traversed.

For the reasons given above, claim 6 of Watanabe Us in view of Patani does not render claims 11 and 14-21 unpatentable. There is nothing in Watanabe US regarding the criticality of the pH of the reaction. Therefore, one skilled in the art, reading Watanabe in view of Patani, would not be led to adjusting the pH of the reaction to maximize yield and purity of the desired products.

In view of the above, it is respectfully submitted that the claims are now in condition for allowance, and favorable action thereon is earnestly solicited.

Respectfully submitted,

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